

## Abstracts

A207

The last observation carried forward (LOCF) analysis overlooks the meaningfulness of dropout in clinical trials. For antipsychotic medication dropout is an important outcome since long-term treatment is often required and dropout may relate to lack of drug tolerability. **OBJECTIVE:** The current analysis applies the “pattern mixture” approach (Shih & Quan, 1997) in which a composite hypothesis is tested that consists of the probability that there is a difference in completion rates (d) between two drugs and the probability that there is a difference in efficacy of complete cases (e) [ $p = p(d) \times p(e) \times (1 - \ln(p(d) \times p(e)))$ ]. **METHODS:** The pattern-mixture approach was applied to data from a 53-week randomized, open-label non-inferiority efficacy trial of risperidone long-acting injectable (RLAI) vs. olanzapine tablets (OLA) in treating schizophrenia (n = 618) (data on file JNJ). **RESULTS:** LOCF had found a significant difference ( $p = 0.04$ ) on percent of patients in each group who attained clinical improvement (20% improvement on PANSS total) favoring RLAI and no significance on difference in the continuous measure of change in PANSS total ( $p = 0.83$ ). Among completers there was a greater decline on change in PANSS total favoring RLAI (Ris  $-23.6(\pm 14.4)$ ; Ola  $-21.9(\pm 18.0)$ ; 1-tailed  $p = 0.105$ ). 76% of the RLAI treated patients completed the trial as compared to 70% of the OLA treated patients (one-tailed  $p = 0.087$ ). Using the pattern mixture approach the probability for the combined hypothesis of a difference in efficacy in complete cases, and trial completion, was significant ( $p = 0.05$ ). On clinical improvement, 66.1% of RLAI group both completed the trial and improved as compared to 53.7% of the olanzapine group (Odds Ratio [95% Confidence interval]: 1.84 [1.20:2.82]). **CONCLUSIONS:** LOCF may not capture real-life, clinically important differences which can be captured by other approaches.

PMH37

#### THE ECONOMIC BURDEN OF SCHIZOPHRENIA IN THE UNITED STATES IN 2002

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**OBJECTIVES:** This study quantifies excess annual costs associated with schizophrenia patients in the United States in 2002 from a societal perspective. **METHODS:** Annual direct medical costs associated with schizophrenia were estimated separately for privately (n = 1090) and publicly (Medicaid n = 14,074) insured patients based on administrative claims data, including a large private claims database and a State Medicaid database, and compared separately to demographically-geographically matched control samples (1 case: 3 controls). Medicare costs were imputed using the Medicare/Medi-Cal dual eligible patients (n = 1491) and published statistics. Excess annual direct non-health care costs were estimated for law enforcement, homeless shelters, and research/training related to schizophrenia. Excess annual indirect costs were estimated for four components of productivity loss: unemployment, reduced work place productivity, premature mortality from suicide, and family care giving using a human capital approach based on market wages. All costs were adjusted to 2002 dollars using the Consumer Price Index and were based on the reported prevalence in the National Comorbidity Survey Replication. **RESULTS:** The overall US 2002 cost of schizophrenia was estimated to be \$62.7 billion, with \$22.7 billion excess direct health care cost (\$7.0 billion outpatient, \$5.0 billion drugs, \$2.7 billion inpatient, \$8.0 billion long term care). The total direct non-health care excess costs, including living cost offsets, were estimated to be \$7.6 billion. The total

indirect excess costs were estimated to be \$32.4 billion. **CONCLUSION:** Schizophrenia is a debilitating illness resulting in significant costs. The indirect excess cost due to unemployment is the largest component of overall schizophrenia excess annual costs.

PMH38

#### A DISCRETE EVENT SIMULATION (DES) MODEL TO DESCRIBE SCHIZOPHRENIA

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The prevalence of schizophrenia varies between 0.2–1% and the cost to treat patients is substantial. Modeling a schizophrenic population is demanding since schizophrenia is a life long disease during which patients go through many states and the transition from one state to another is dependent on the history of patients. A previously built 1st order Monte Carlo DES model was adapted to enable 2nd order Monte Carlo simulation. **OBJECTIVE:** This abstract describes why and how the model was upgraded from a 1st order Monte Carlo (MC) simulation to a 2nd order MC model. The abstract will describe the choices made in the design of the model, the internal validity and evaluation of its strengths and weaknesses. **METHODS:** Internal validity of the model has been explored using data from several patient databases, as well as literature on a list of variables, including PANSS, the proportion of patients institutionalized and costs. Pert, beta, lognormal and uniform distributions have been used to describe 2nd order uncertainty of relevant variables, such as PANSS, QALY, risk and costs. **RESULTS:** The model was programmed to reflect the PANSS at 0 year, 1 year, and 5 years for patients from the considered databases. The modeled annual cost per patient and the location distribution were similar to published data. Outcomes were expressed in terms of direct medical costs, number and duration of episodes, PANSS, QALY, GAF, CGI, SF36 and the SF6 mental component. The uncertainty surrounding the outcomes of costs and effect measures were assessed with acceptability curves and ellipses. **DISCUSSION:** The original DES model was vastly improved with the use of additional database analyses, additional correlation analyses and 2nd order Monte Carlo simulations. This has resulted in less emphasis on expert opinion, yielding a partially validated probabilistic model which can be adapted for numerous health care settings.

PMH39

#### ARE QALYS SUITABLE FOR SCHIZOPHRENIA TRIALS?

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**OBJECTIVES:** The utility of quality adjusted life years (QALYs) as an evaluative tool in clinical psychiatric research and drug trials relating to schizophrenia has rarely been tested due to the many limitations surrounding its use. The limitations include lack of comprehensive models of quality of life specific to schizophrenia, unavailability of appropriate measures sensitive enough to pick up small changes that are expected in the course of the illness, and lack of adequate information about the performance of available instruments. **METHODS:** This paper reviews currently available evidence on the use of QALYs in studies of people with schizophrenia examining the relationship

between QALY scores and scores on instruments regularly used in schizophrenia studies such as the PANSS or the CGI, in order to see if it is possible to construct reliable 'crosswalks' between such clinical measures and the QALY-generating scores. **RESULTS:** The limited evidence in the field suggests that the calculation of QALYs to quantify the adverse effects of schizophrenia is difficult. Nevertheless, usefulness of such calculation for a proper estimation of the true burden of schizophrenia cannot be ignored. Data from a large observational study, following 600 people with schizophrenia over three years, are used to analyse the correlation between utility-generating scores from EQ-5D and schizophrenia specific measures of clinical circumstances such as the PANSS, the MADRS, the AIMS measure of side effects, the Simpson-Angus measure of side effects and the Barnes Akathisia Rating Scale to see how generic instruments such as EQ-5D perform in evaluating different health states in Schizophrenia. **CONCLUSIONS:** Although the EQ-5D index does not capture the changes in quality of life associated with symptoms changes, it may be reasonably valid for calculating QALYs for patients with schizophrenia.

## PMH40

**LONG-TERM MAINTENANCE OF INITIAL HEALTH RELATED QUALITY OF LIFE (HRQL) IMPROVEMENTS GAINED THROUGH ANTIPSYCHOTIC TREATMENT: 24-MONTH RESULTS FROM THE SCHIZOPHRENIA HEALTH OUTCOMES (SOHO) STUDY**

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**OBJECTIVES:** 1) To describe the long term evolution of HRQL of outpatients with schizophrenia, and 2) to analyse its association with antipsychotic use. **METHODS:** SOHO is an ongoing, 3-year, observational study of the treatment of schizophrenia in ten European countries. The primary objective of SOHO is to assess the costs and outcomes of treatment of schizophrenia using antipsychotics. Together with clinical measures, the EQ-5D (VAS score and tariffs) were administered at baseline, and 3, 6, 12, 18, and 24 months. The 'panel analysis' approach was used, since the outcomes were measured for the distinct post baseline epochs (0–6, 6–12, 12–18, and 18–24 months of treatment). Multivariate modeling was performed for each epoch, adjusting for baseline differences among patients. When using the second and subsequent episodes of patient treatment the baseline covariates were derived from the covariates collected when the patient switched treatment. **RESULTS:** A total of 8109 patients were included in this analysis (44% women; mean age: 40); 24-month retention was 78.47%. Overall, the EQ-5D score after each period of continuous treatment was: Baseline; mean 0.6 SD 0.32; (0–6 months): 0.76 SD 0.26; (6–12 months): 0.79 SD 0.24 (12–18 months): 0.81 SD 0.23; (18–24 months): 0.82 SD 0.23. Olanzapine-treated patients had statistically higher EQ-5D utility improvements during the first 6 months compared with risperidone (difference in mean change: 0.041; 95% CI: 0.023–0.06)-, quetiapine (0.032; 0.006–0.059)-, oral (0.081; 0.057–0.105)- and depot typicals (0.077; 0.049–0.105)-treated patients. No statistical separation was observed between olanzapine, clozapine and amisulpride groups. These differences remain during the 24-month follow-up. **CONCLUSIONS:** Antipsychotic treatment is associated with sustained improvement in HRQL. The improvements in EQ-5D scores during the first 6 months for the Olanzapine group were significantly higher than the improvement for other antipsychotics and remaining thereafter, with the exception of Amisulpride and Clozapine where no significant separation was found.

**REMISSION CRITERIA FOR DEPRESSION WHEN USING SHORT VERSIONS OF THE HAMILTON DEPRESSION RATING SCALE (HDRS)**

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**OBJECTIVES:** To define criteria for symptoms remission in depression for reduced versions of the HDRS. **METHODS:** The discriminative validity of the HDRS (HDRS-21 and 17 items) and its shorter scales [Bech Melancholia Scale (BMS-6); Maier & Philips Severity Scale (MPSS-6); Gibbons et al Depression Scale (GDS-8); Evans et al Depression Scale (EDS-6)], was assessed against the Clinical Global Impression of severity (CGI) in a Spanish multicenter study. The study included 168 depressive patients in ambulatory care. Of these, 118 patients were considered as clinically unstable (either because of presenting a new/recurrent disease episode or because of needing an adjustment/change of treatment). After six weeks, those patients were reassessed by the HDRS and the CGI. The best cut-off points to discriminate the criterion of clinical remission (CGI score = 1) were found by using Receiver Operating Characteristic analyses (ROC). The accuracy of the different versions was assessed by analysing the area under the ROC curves (AUC). **RESULTS:** All versions discriminated at baseline the severity of depression according to the CGI criterion (all p-values < 0.005 by one-way ANOVA corrected for multiple comparisons). Also, all versions discriminated the severity of depression (remission versus no remission) at six weeks of follow-up (all p-values < 0.0001 by t-test analyses). The ROC analyses suggested the following cut-off points to identify remission criteria in our sample (HDRS-21: <=7; HDRS-17: <=7; BMS: <=2; MPSS: <=3; GDS: <=5; EDS: <=4). The AUC showed similar accuracy for the HDRS-21, HDRS-17 and the four shorter versions (AUC range from 0.89 to 0.95, chi2 (five df) = 8.72, p = 0.12). **CONCLUSION:** Compared with the canonical versions of the HDRS (21 or 17 items), shorter versions have showed similar accuracy to define remission of depressive symptoms.

## PMH42

**COMPARISON OF SSRI AND SNRI TREATMENT FOR DEPRESSION IN PRIMARY CARE: A NATURALISTIC STUDY**

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**OBJECTIVES:** To compare outcomes of patients receiving either SSRI or SNRI antidepressants for Major Depression in primary-care settings. **METHODS:** We analyzed data collected from an observational study in 47 primary care facilities in four Canadian provinces. Patients meeting DSM-IV-TR criteria for major depression, >=18 years of age and scoring >=18 on the HAMD-17 were assigned to groups assessed using HAMD-7 or HAMD-17. All patients received SSRIs or SNRIs according to their physician's preference. Patient outcome was remission (HAMD-17 <=, or HAMD-7 <=) after 8 treatment weeks. **RESULTS:** Of the 337 patients, 159 (47.2%; 66.6% were females) received SSRIs (citalopram-110, fluoxetine-9, paroxetine-37 and sertraline-3), and 178 (52.8%, 67.4% were females) received SNRIs (venlafaxine-XR). Mean age was 42.0 ± 13.6 for SSRIs and 43.7 ± 13.7 for SNRIs (P = 0.60). SSRI-treated